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Original article

Bacteriology profile of febrile infectious complications after transrectal ultrasound-guided prostate biopsy

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ABSTRACT

Objective: Infection and fever are a major issue of transrectal ultrasound (TRUS)-guided prostate biopsy related complications. The aim of the present study is to evaluate the incidence and bacteriology profile of infectious complications and fever after prostate biopsies.
Materials and Methods: A total of 5027 patients underwent prostate biopsy from July 2005 to December 2010 at our center. Three different prophylactic antibiotic protocols were administered 20 minutes before biopsy. The choice of protocols was according to the attending physician's preference. Patient data were reviewed for prostate pathology, medical comorbidities, risk factors for urosepsis, use of prophylactic antibiotics, causative organisms, and antibiotic sensitivity patterns in both blood and urine cultures.
Results: Seventy patients (1.39%) developed fever after biopsy. The average age was 71 years, the average calculated weight of the prostate was 50.5 ± 22 g, and the median prebiopsy prostate-specific antigen (PSA) level was 8.48 ng/mL. Among 21 urine-positive patients, seven (33.3%) urine cultures yielded *Escherichia coli* (*E. coli*) and 10 (47.6%) yielded Gram-negative bacilli. None of the patient factors or coexisting comorbidities, prebiopsy pyuria, or prostate cancer, was significantly associated with the development of fever after biopsy. There was no significant difference between each group of prophylactic antibiotic protocols.
Conclusion: Our study demonstrated an overall postbiopsy febrile complicating infection rate of 1.39%. *E. coli* was the most common pathogen. Fluoroquinolones or second generation cephalosporins are suggested as the initial choice in patients with postbiopsy fever.

1. Introduction

Prostate cancer is the fifth most common cancer in Taiwanese men.[1] Prostate cancer is primarily diagnosed through prostate needle biopsy, commonly performed using the transrectal ultrasound (TRUS)-guided technique. This technique is frequently employed in urological departments worldwide and is considered a safe practice.

Major complications are rare, but there are frequent minor complications. The most common risks and complications associated with TRUS-guided biopsy include infection, hematuria, urinary retention, and hematochezia.[2,3] Infectious complications can be severe, requiring hospitalization,[4] and include fever, urinary tract infection, acute bacterial prostatitis, epididymo-orchitis, and sepsis.[5]

To prevent these infections, broad-spectrum oral antibiotics with or without bowel preparation have been used. Antibiotic prophylaxis is universally used and numerous protocols have been described.[6] The American Urological Association (AUA) Best Practice Statement for antibacterial prophylaxis recommends use of a fluoroquinolone as a first line therapy for the prevention of infection from transrectal prostate biopsy.[7] However, some patients develop fever after biopsy despite the use of antibiotics. The infection rate in larger studies has been estimated at 0.1–7%.[5,8–14] To date, quinolone has been recommended as the prophylactic protocol in practice in Taiwan, but has not been ubiquitously adopted. The aim of the present study was to evaluate the incidence and bacteriology profile of infectious complications and fever after prostate biopsies.

2. Materials and methods

We retrospectively reviewed patients who underwent TRUS-guided biopsy of the prostate from July 2005 through December 2010 at Taipei Veterans General Hospital.

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The majority of biopsies were performed by resident urologists. An Evac enema (118 mL/bottle) was administered about 1 hour before biopsy. The enema was repeated if stool was palpated on digital rectal examination. The biopsy procedure was performed without anesthesia. Acetylsalicylic acid or oral anticoagulant agents were withdrawn 7–10 days before biopsy, after approval by the prescribing physician.

The patient received one of the following prophylactic antibiotic protocols: (1) single intramuscular injection of gentamicin (80 mg) before biopsy followed by oral cefadroxil (500 mg) every 12 hours for 5 days after biopsy; (2) single intravenous injection of cefazolin (1000 mg) followed by oral cefadroxil (500 mg) every 12 hours for 5 days after biopsy; or (3) oral pipemidic acid (250 mg) every 12 hours for 3 days from the day before biopsy. Selection of the prophylactic protocol was made according to usual practices of the physicians.

The prostate volume and transition zone volume were measured, and a 12-core, or double sextant, biopsy was performed uniformly with the patient in the left lateral decubitus position.

Patient data were reviewed for prostate pathology, medical comorbidities, risk factors for urosepsis, use of prophylactic antibiotics, causative organisms, and antibiotic sensitivity patterns in both blood and urine cultures.

Fever was defined as an ear temperature >38°C. A nonfever group of patients was selected as the control group. For one patient who developed fever after biopsy, the control group was composed of two patients who underwent the same prophylactic antibiotic protocol and did not develop fever after biopsy. The control group was selected by simple random selection.

These groups were compared with respect to descriptive characteristics and factors using a *t* test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. All variables with suggestive *p* values on univariate analysis were included in the multivariate analysis, and $p \leq 0.05$ was considered statistically significant.

3. Results

From July 2005 through December 2010, 5027 patients underwent prostate biopsy. Of these, 4252 received Protocol 1 (intramuscular gentamicin), 403 Protocol 2 (intravenous cefazolin), and 372 Protocol 3 (oral pipemidic acid) as prophylactic antibiotic therapy.

Seventy patients (1.39%) developed fever after biopsy. One patient was admitted to the intensive care unit, and there was no infection-related mortality. Regarding the characteristics of patients who developed fever after biopsy, the average age was 71 years, the average calculated weight of the prostate was 50.5 ± 22 g, and the median prebiopsy prostate-specific antigen (PSA) level was 8.48 ng/mL (Table 1).

Table 1
Patient characteristics.

	Fever ($n = 70$)	Non-fever ($n = 140$)
Age (y)	71.1 ± 8.6	74.4 ± 10.0
≤65 [*n*, (%)]	20 (28%)	24 (17%)
65–80	41 (59%)	77 (55%)
>80	9 (13%)	39 (28%)
Prostate size (cm^3)		
Inner gland	21.0 ± 13.1	20.1 ± 13.2
Outer gland	50.5 ± 22.2	45.8 ± 22.3
Inner/outer ratio (%)	40.5 ± 15.6	43.2 ± 16.7
PSA [median (IQR)] (ng/mL)	8.48 (5.55–13.6)	8.515 (6.205–13.11)
Biopsy proved prostate cancer	20 (28.6%)	44 (31.4%)
WBC count at presentation ($/mm^3$)	11,017 ± 6360	
<4500 [*n*, (%)]	5 (7.6%)	
4500–11,000	33 (50%)	
>11,000	28 (42.4%)	

IQR = interquartile range; PSA = prostate-specific antigen; WBC = white blood cell.

Table 2
Bacteria culture result.

	Urine	Blood
Escherichia coli	7 (33.3%)	19 (86.4%)
Gram-negative bacilli (colony < 10^4/mL)	10 (47.6%)	–
Klebsiella pneumoniae	1 (4.7%)	2 (9.1%)
Proteus spp.	1 (4.7%)	1 (4.5%)
Acinetobacter baumannii	1 (4.7%)	–
Gram-positive cocci	1 (4.7%)	–

Of the 70 fever patients, 21 (30.0%) had positive urine culture results and 22 (31.4%) had positive blood culture results. Overall, 36 patients (51.4%) had a positive culture result for either urine or blood. Among 21 urine-positive patients, 7 (33.3%) urine cultures yielded *Escherichia coli* (*E. coli*) and 10 (47.6%) yielded Gram-negative bacilli (GNB). The urine culture result would be reported GNB if the colony count was $<10^4$/mL. Other isolated organisms included *Klebsiella pneumoniae* (*K. pneumoniae*), *Proteus* spp., *Acinetobacter baumannii*, and Gram-positive cocci (GPC). Of the blood cultures, 19 (86.4%) yielded *E. coli*, two yielded *K. pneumoniae*, and one yielded *Proteus* spp. (Table 2).

Resistances of all identified bacteria, including from blood and urine, were as follows: first generation cephalosporin ($n = 5$, 17.9%), second generation cephalosporin ($n = 3$, 10.7%), gentamicin ($n = 7$, 24.1%), trimethoprim-sulfamethoxazole ($n = 14$, 70%), ampicillin ($n = 22$, 75.9%), and ciprofloxacin/levofloxacin ($n = 3$, 10.3%) ($p < 0.001$) (Fig. 1).

Of all derived *E. coli* cultures, quinolone-resistant *E. coli* was isolated in two (7.7%); one from blood and one from urine. The blood culture was obtained in 2006 and the urine in 2009. Both patients were treated with a fourth generation cephalosporin and were discharged uneventfully.

Most fever patients ($n = 49$, 70%) developed signs within 48 hours of the biopsy. Thirteen patients (18.57%) exhibited fever 48–72 hours after biopsy, and only eight (11.43%) patients developed fever after 72 hours.

Among the three prophylactic antibiotic protocols, the majority of patients underwent Protocol 1 (single dose of intramuscular gentamicin). There was a lower fever rate in patients who underwent Protocol 1 than in patients who underwent the other two protocols. However, there was no significant difference between each group (Fig. 2). The fever rate was as follows: Protocol 1, 1.27% ($n = 54$); Protocol 2, 2.19% ($n = 9$); Protocol 3, 1.85% ($n = 7$).

Risk factor analysis disclosed that none of the patient factors or coexisting comorbidities, including age, diabetes mellitus, hypertension, chronic renal insufficiency, prebiopsy pyuria, or prostate cancer, was significantly associated with the development of fever after biopsy (Table 3).

4. Discussion

TRUS-guided biopsy is the standard procedure for histological diagnosis of prostate cancer. In the present study, 1.39% of the

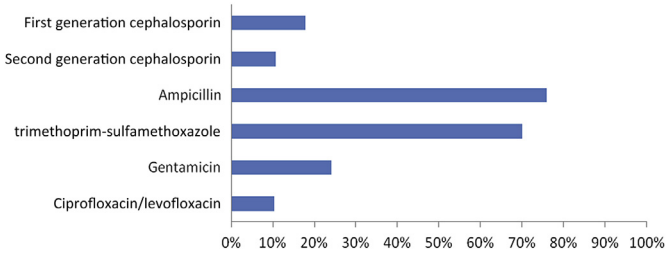

Fig. 1. Antibiotic resistance rates of all cultured bacteria.

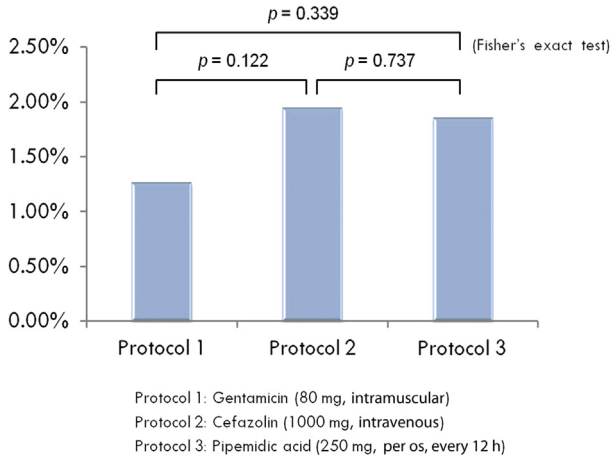

Fig. 2. Fever rates of three different prophylactic antibiotic protocols.

patients developed fever after TRUS-guided biopsy. Risk factor analysis revealed no significant difference. No statistical difference was noted among the three prophylactic protocols.

The proposed mechanism of infection involves fecal contamination seeding the bladder and vasculature following passage of the biopsy needle through the rectal mucosa. The most common isolated pathogen in our study was *E. coli*, which concurred with the results of many previous studies.[4,5,14–17] Approximately 90% of fever patients developed signs within 72 hours of biopsy, and all of the fever patients had signs within 1 week. These are useful data for our clinical practice and for patient education.

No significant risk factor was identified in our study for febrile infectious complications after TRUS-guided biopsy. Lindert et al[18] reported that age, PSA level, urinary tract infection history, AUA symptom score, prostate volume, cancer, and number of biopsies did not predict problems after biopsy. Chiang et al[6] also reported that age, underlying disease, increased biopsy core number, and antiplatelet/anticoagulant usage were not associated with major complications after prostate biopsy. Many study results are similar to the above-mentioned results.

Although our study disclosed a lower postbiopsy febrile complicating infection rate in the gentamicin prophylaxis group, the difference did not reach statistical significance. Certain studies have demonstrated that fluoroquinolones are superior to gentamicin with both lower fever and bacteremia rates,[19] and others have suggested that levofloxacin appeared superior to pipemidic acid.[6] Although quinolones have been widely accepted as the first choice of prophylactic antibiotic for TRUS-guided prostate biopsy, Adibi and colleagues[20] recently reported that addition of gentamicin to current prophylactic regimens significantly reduced the rate of hospitalization for postbiopsy infectious complications.[21] Along with our data, gentamicin thus may act as an alternative or adjunct antibiotic of quinolones prophylaxis.

Table 3
Univariate analysis of TRUS biopsy risk factors.

	Fever	Non-fever	*p* value
Age	71.1 ± 8.6	74.4 ± 10.0	0.693
Renal insufficiency	5 (7.1%)	8 (5.7%)	0.686
Hypertension	33 (47.1%)	70 (50.0%)	0.696
Steroid use	1 (1.4%)	1 (0.7%)	0.615
Diabetes mellitus	9 (12.9%)	23 (16.4%)	0.436
Prebiopsy pyuria	6 (8.6%)	11 (7.9%)	0.858
Biopsy proved prostate cancer	20 (28.6%)	44 (31.4%)	0.672

Increasing rates of bacterial resistance to fluoroquinolones have been reported worldwide in recent years, with at least 20% ciprofloxacin resistance among *E. coli* isolates in urine samples.[14,17,21] In our study, two cases of ciprofloxacin-resistant *E. coli* were isolated, one from urine and the other from blood, accounting for 8.7% of all positive *E. coli* cultures. This resistance rate is lower than that reported in other countries. A possible explanation is that the majority of patients at our hospital receive non-fluoroquinolone antibiotics as prophylaxis. In our study, fluoroquinolone and second generation cephalosporins had lower resistance rates among all isolates. Thus, these agents may be useful antibiotic choices in patients with fever after biopsy.

There are several limitations in our study. The major limitation is that this was a single-center retrospective study. The marked population difference between the gentamicin prophylaxis group and the other two groups needs to be noted. Further, individual patient variations in health status, such as renal insufficiency and drug allergy, resulted in prophylactic antibiotic alterations.

5. Conclusion

Our study demonstrated an overall postbiopsy febrile complicating infection rate of 1.39%. *E. coli* is the most common pathogen. Fluoroquinolone or second generation cephalosporin is suggested as the initial choice in patients with postbiopsy fever.

Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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